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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,412	01/29/2004	Stephen A. Johnston	UTSD:681USC1	2869

32425 7590 04/19/2007
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EXAMINER	
LIU, SUE XU	
ART UNIT	**PAPER NUMBER**
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/767,412	JOHNSTON ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-63* is/are pending in the application.

4a) Of the above claim(s) *42,46 and 61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41, 43-45, 47-60, 62 and 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/1/07 has been entered.

Claim Status

2. Claims 1-40 have been canceled.

Claims 41-63 are currently pending.

Claims 42, 46, and 61 have been withdrawn.

Claims 41, 43-45, 47-60, 62, and 63 are being examined in this application.

Claim Amendments

3. The amendment and response filed on 2/1/07 has been fully considered and entered in the application.

Election/Restrictions

4. Applicant's election with traverse of Groups I and II (Claims 41-63) in the reply filed on 9/12/2005 is as previously acknowledged.

5. Applicant's election **without** traverse of the following species in the reply filed on 9/12/2005 is as previously acknowledged. Applicants elected: A: mouse; B: human; C: bacterial cell; D: E.coli; E: human growth hormone; H: about 400bp.

Priority

6. This application claims benefit as a continuation of U.S. Application Ser. No. 09/448,330, filed November 22, 1999 (abandoned on 3/26/2004); which application is a divisional of U.S. Application Ser. No. 09/001,157, filed December 30, 1997, now issued as U.S. Patent No. 5,989,553; which application is a divisional of U.S. Application Ser. No. 08/421,155, filed April 7, 1995, now issued as U.S. Patent No. 5,703,057.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosures of the prior-filed applications, Applications No. 09/448,330, 09/001,157, and 08/421,155, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

Claim 41 has been amended to recite, in step iii), "performing *in vivo* selection of at least a first member from the library that elicits an immune response to identify said nucleic acid or antigen", as filed on 2/1/07. The amended claim reads on a method step of selecting one single member from the introduced library within the one animal (i.e. "in vivo" selection), and the selection is based on one single member's ability to elicit "an immune response". This method step is not specifically disclosed in the claimed priority applications.

Thus, the subject matter recited in Claim 41 and its dependent claims do not obtain the earlier filing date.

The effective filing date of the said subject matter is 1/29/2004.

Claim Rejections Withdrawn

7. In light of applicants' amendments to the claims, the following claim rejections in the previous office action are withdrawn:

A.) Claims 41, 43, 44, 48-52, 54-60 and 62 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 and 27-30 of U.S. Patent No. 5,703,057.

Claim Rejections Maintained

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

9. Claims 41, 43-45, 47-60, 62 and 63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The previous rejection is maintained for the reasons of record advanced on pages 4-6 of the office action mailed on 10/28/2005.

Discussion and Answer to Argument

10. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue that the instant claims have been misinterpreted. Specifically, the previous action erred in asserting that "it is a nucleic acid that elicits an immune response, rather than an antigen encoded by a nucleic acid". Applicants further assert that the instant

claims recite a method for "identifying a nucleic acid from a library that codes for an antigen that elicits an immune response, and/or the encoded antigen." (Reply, p. 5, para 3)

However, the instant claims (Claim 41) recite "wherein the nucleic acid or antigen has been determined to elicit an immune response ..." (Step (a) of Claim 41), and "a first member from the library that elicits an immune response ..." where the library is a nucleic acid library (Step (a) (iii) of Claim 41).

The straightforward interpretation of the above underlined recitation would be "the nucleic acid ... elicit an immune response".

In addition, the instant specification does not specifically define the term "antigen", which can be a nucleic acid, a protein, a small molecule, etc.

Furthermore, regardless which entities (the nucleic acid or the protein) that elicit the immune response, applicants have not demonstrated possession of the entire claimed genus of "nucleic acid", or "antigen" from any pathogen that can elicit an immune response in a subject (e.g. an animal or a human), and be used as a vaccine in a subject.

Applicants also argue the specification lists numbers of species (22 different species of "pathogens"), and thus applicants are in possession of the entire claimed genus of pathogens to use in the claimed method of screening and vaccination. (Reply, pp. 6-7)

To address applicant's argument, the claim language is very broad and encompasses any organism that constitute as a pathogen, which is reflected by the instant specification as pointed out by the applicants (Reply, p. 6, the bolded and underlined citations). Even though the instant specification recites two particular examples of organisms, from which the library of nucleic

acids can be derived from, these organisms are different species of bacteria. The term pathogen encompasses an entire genus of vast numbers of organisms (such as viruses and fungi) that are different in structure and/or functions. As applicants have pointed out under MPEP 2163 (II)3,

> Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, e.g., Eli Lilly. Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces.
> (emphasis added)

a show of possession of the claimed entire genus of "pathogens" through representative number of species must demonstrate common attributes or features of the claimed genus. The two examples of the bacteria species do not share common structures and/or functions with the other species (such as viruses and fungi) within the claimed genus of pathogens.

Applicants also asserted that the Office "should be able to explain what number would be representative" and that "No such basis or number has been provided" (Reply, p. 7). Contrary to applicant's assertion, the previous Office action has addressed the issue of "a representative number of species" (Office action, mailed 8/1/06, pp. 4-5). As discussed previously and above, the instant claims are drawn to **any** pathogen, and vaccinating any subject with a nucleic acid or an antigen. Either a common structure or a representative number of species must be provided to indicate possession of the claimed genus. The term pathogen encompasses a variety of organisms with different structures and/or functions such as different genomes, different protein compositions, etc. For example, one of ordinary skill in the art would not be able to immediately

envisage a "virus" by studying the structure of a "bacteria". That is a disclosure of a bacteria would not be a representative number of species of the claimed genus of "pathogen".

Applicants also seem to argue that all of the pathogens possess "genomic material", and thus a common structure has been demonstrated. (Reply, p. 7, para 2+). By applicant's argument, all animals, plants, microorganisms, etc., can constitute as one genus, and a disclosure of a bacteria species can be used to represent a human species. Certainly, an ordinary skilled artisan cannot envisage a human from a bacterium. Applicants also argue "the claims and specification convey a functional aspect of the claimed genus to a person of skill in the art in a manner that satisfies the written description requirement" (Reply, p. 8, para 1; emphasis added).

> "A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." Eli Lilly, 119 F.3 at 1568, 43 USPQ2d at 1406. See also Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991))."
> (MPEP 2163; emphasis added)

As discussed above, to show possession of a chemical entity (such as a nucleic acid or antigen), structures, physical properties need to be disclosed. For example, a vaccine based on a nucleic acid (with specific sequence and structure) for protection against a "Mycoplasma" species would certainly not provide protection against HIV (a "pathogen" listed in the instant spec.), which does not have a known successful vaccine at least for human as of the mailing date of the instant Office action.

In addition, merely providing a "laundry list" of species do not convey possession of the entire genus. See MPEP 2163 I:

> "A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559,

> 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967)"
> (emphasis added).

In addition, the case laws have addressed the issues of written description for methods using compounds that are yet to be identified.

> "An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.")."
>
> MPEP 2163. (emphasis added).

In this case, neither the instant specification nor the claims provided any specific antigen or a nucleic acid encoding a specific antigen that is used to "vaccinate" a subject against a particular "pathogen". The instant specification at best only described "a wish or plan for obtaining" a nucleic acid or an antigen for vaccinating a subject against a specific pathogen. Similar to the Rochester case, the instant disclosure has not demonstrated possession of the claimed nucleic acid or antigen for vaccinating a subject against a particular disease caused by a particular pathogen. Applicant's claimed scope represents only an invitation to experiment regarding possible vaccines.

Therefore, the instant specification has not provided specific core structure or representative numbers of species to demonstrate the possession of the entire genus of pathogens, and/or nucleic acids or antigens from the pathogens that can be used as vaccines.

Applicants also asserts "The new ELI method combines the advantages of genetic immunization ***without the necessity of discovering a single protective gene or foreknowledge of the pathogen's biology****." (Reply, p. 8, para 1; emphasis provided by applicants).*

The above quoted statement from applicant's reply further provides evidence that the instant disclosure has not demonstrated possession of "the nucleic acid or antigen" that can be administered to "a subject" to "effectively" "vaccinate the subject against the pathogen". From the above quoted statement, it is clear that "a single protective gene" (i.e. the nucleic acid) is not in possession to use as an effective vaccine for protection against a specific pathogenesis. In addition, the above statement also seems to be contrary to the recitation of "identify said nucleic acid or antigen" of the instant Claim 41, which requires the identification of a specific nucleic acid (or a gene).

Applicants also assert that the instant disclosure demonstrates possession of the claimed genus of "subject" and "animal". (Reply, pp. 8-9).

Similar to the discussion above regarding the possession of claimed entire genus of pathogens, nucleic acids, and/or antigens, the instant specification also has not demonstrated the possession of the entire genus of subjects, which could be any animal (including human). Similarly to the discussion regarding the claimed genus of pathogens, only one species (mouse)

of the claimed genus of subjects is disclosed by the instant specification. The claimed genus of subjects encompasses any animals and human. The different animals would not share common attributes and/or features that would render one single example representative of the entire genus of subjects (animals). For example, a vaccine developed for an animal such as a mouse would not necessarily be applicable for human subjects. Therefore, the instant specification has not provided representative number of species to demonstrate the possession of the entire genus of subjects.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 41, 43, 48, 50-60 and 62 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 52-65 of copending Application No. 10/023,437. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. The previous rejection is maintained for the reasons of record advanced on pages 7-9 of the office action mailed on 10/28/2005.

13. Claims 41, 43, 59-60, 62 and 63 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of U.S. Patent No. 6,410,241 B1 (henceforward refers to as '241 patent). The previous rejection is maintained for the reasons of record advanced on pages 7-9 of the office action mailed on 10/28/2005.

Discussion and Answer to Argument

14. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants "generally traverse, but not that a terminal disclaimer wil be submitted upon indication of allowable subject matter". (Reply, p. 9).

Applicant's intention to submit Terminal Disclaimers to overcome the ODP rejections over the above said application and patents is acknowledged. However, applicants have not filed any Terminal Disclaimer to overcome the ODP rejections, and thus the rejections are maintained for the reason or record.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Lai et al

16. Claims 41, 43-45, 47-50, 54-56, 59 and 62 are rejected under **35 U.S.C. 102(b)** as being anticipated by Lai et al (Vaccine. Vol 12: 291-298; March, 1994). The previous rejection is maintained for the reasons of record advanced on page 10 of the office action mailed on 10/28/2005.

Discussion and Answer to Argument

17. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue that the amended claims (Claim 41) recite "in vivo selection", which is not taught by the Lai reference.

Contrary to applicant's assertion, the Lai reference does teach a method including the step of "in vivo selection" (Step (a) iii) of Claim 41). First, the instant claim language can be interpreted to mean a determination of an immune response cause by a plurality ("at least a first

member") of members that are the same nucleic acid in an animal. The instant claim language does not dictate that the actual determination of the identity of the nucleic acid or antigen is carried out *"in vivo"* (i.e. inside the animal).

Lai et al teach screening a library of DNA constructs derived from *Mycoplasma pulmonis* (MP; a bacterial pathogen), and immunizing animals with selected constructs against MP (See Abstract). The reference teaches injecting bacterial suspension (containing plurality of plasmid constructs) into mice and eliciting an immune response (Page 293, 2nd paragraph), which reads on administering a plurality of nucleic acids to a subject (or animal) and eliciting an immune response for the in vivo selection step. The reference also teaches selecting four clones (page 293, 1st paragraph), and sequencing analysis to identify the insert in the plasmid construct (Page 295), which reads on identifying the nucleic acid.

Coney et al

18. Claims 41, 45, 47, 48, 59, 60 and 62 are rejected under **35 U.S.C. 102(a)** as being anticipated by Coney et al (Vaccine. Vol 12: 1545-1550. 12/1994). The previous rejection is maintained for the reasons of record advanced on pages 11-12 of the office action mailed on 10/28/2005.

Discussion and Answer to Argument

19. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue that the amended claims (Claim 41) recite "in vivo selection", which is not taught by the Lai reference.

Contrary to applicant's assertion, the Coney reference does teach a method including the step of "in vivo selection" (Step (a) iii) of Claim 41). First, the instant claim language can be interpreted to mean a determination of an immune response cause by a plurality ("at least a first member") of members that are the same nucleic acid in an animal. The instant claim language does not dictate that the actual determination of the identity of the nucleic acid or antigen is carried out *"in vivo"* (i.e. inside the animal).

Coney et al, teach several constructs encoding various HIV that were administered to mice, as taught by Coney et al (page 1546, right column, 3rd paragraph of the Coney reference), read on a library comprising DNA or RNA sequence from a pathogen. The several constructs taught by Coney would constitute a plurality, hence, a library of multiple sequences.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. Claims 41, 43-45, 47-60, 62 and 63 are rejected under 35 U.S.C. 103(a) as being obvious over Lai et al (Vaccine. Vol 12: 291-298; March, 1994), in view of Felgner et al (US Patent No.

5,589,466). The previous rejection is maintained for the reasons of record advanced on pages 12-14 of the office action mailed on 10/28/2005.

Discussion and Answer to Argument

22. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants traversed the above rejection with the same argument as the traversal over the Lai reference alone. Thus, applicants are respectively directed to the discussion under the Lai reference for answer to arguments.

New Rejections

Claim Rejections - 35 USC § 112

23. Applicants are respectively directed to the section under the heading "Claim Rejections Maintained" in the instant Office action for the text of those sections of Title 35, U.S. Code.

New Matter Rejection

24. Claims 41, 43-45, 47-60, 62, and 63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 41 has been amended to recite, in step iii), "performing *in vivo* selection of at least a first member from the library that elicits an immune response to identify said nucleic acid or antigen", as filed on 2/1/07. The amended claim reads on a method step of selecting one single member or any number of specific members from the introduced library within the one animal (i.e. "in vivo" selection), and the selection is based on one single member's (or a combination of specific members') ability to elicit "an immune response". This method step is not specifically disclosed in the instant specification as originally filed.

Applicants have pointed to "Example 2" (pp. 49-52) of the instant specification for support of the claim amendment. However, Example 2 does not disclose the said method step of "in vivo" selection of at least one member. In Example 2, the specification discloses injecting libraries, in particular, two "sib libraries", each with >3000 "members" into one animal (p. 50, paras 2-3). After the injection of the library (i.e. multiple members), no "selection" or "identification" of **a** member that induced an immune response is "performed". Thus, Example 2 of the instant specification does not disclose the claimed step (iii) in the instant Claim 41.

If Applicant believes this rejection is in error, applicant must disclose where in the specification support for the entire scope of the amendment(s) and/or new claims can be found. As a result, Claim 41 and its dependent claims represent new matter.

Scope of Enablement Rejection

25. Claims 41, 43-45, 47-60, 62, and 63 are rejected under 35 U.S.C. 112, first paragraph, because the specification,

while being enabling for a method selecting all (or a library or plurality) of the introduced library members in an animal for eliciting an immune response, does not reasonably provide enablement for selecting or identifying individual members (e.g. one single specific polynucleotide or one single specific antigen) that elicit an immune response;

while being enabling for a method of vaccinating a mouse against *Mycoplasma pulmonis* (MP) using libraries (pluralities) of nucleic acids obtained from *Mycoplasma pulmonis*, does not reasonably provide enablement for vaccinating any subject using a single specific nucleic acid member from the MP library, and also does not reasonably provide enablement for vaccinating any other subjects (especially human) using libraries (pluralities) of nucleic acids obtained from any other pathogens as vaccines against the pathogens;

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. §112, first paragraph, have been described *In re Wands*, 8 USPQ2d 1400(1988). They are:

1. The breadth of the claims;
2. The nature of the invention;
3. The state of the prior art;
4. The predictability or lack thereof in the art
5. The level of skill in the art;
6. The amount of direction or guidance present;
7. The presence or absence of working examples;

8. The quantity of experimentation needed.

The breadth of the claims and the nature of the invention

The nature of the claims is a combination of a screening method for a specific "nucleic acid" or "antigen" from a pathogen that can elicit an immune response, and a method of vaccinating a subject against the said pathogen using the identified "nucleic acid" or "antigen". The breadth of the claim seems to encompass any "pathogen", any "nucleic acid" and/or "antigen" from a pathogen, any "subject" (including any animal). The claimed methods are drawn to any method of screening for a "nucleic acid" and/or "antigen" to be used as a vaccine for preventing any type of pathological disease caused by any pathogen. However, the instant specification does not describe any specific "nucleic acid" or "antigen" that can be identified and used as a vaccine to protect "a subject" against "a pathogen". In addition, the instant claim language can be interpreted to encompass a method of identifying an antigen from a pathogen that induced an immune response in one type of animal, and then administering the said antigen into another animal (or even a plant) for protection against the pathogen. For example, the instant claimed method reads on a method of identifying a specific nucleic acid from a Mycoplasma that elicit an immune response in mouse, and then administering the said nucleic acid to a human for protection against the same Mycoplasma.

The state of the prior art and the predictablility or lack thereof in the art

The instant claims can be interpreted to recite a method of screening where a plurality of different members (i.e. a library of different nucleic acids) derived from a pathogen are

introduced into an animal, and a specific "nucleic acid" and/or "antigen" is identified inside the animal (i.e. "*in vivo*") that elicit an immune response. The said identified "nucleic acid" is used to vaccinate a subject against the pathogen. However, the instant specification does not disclose the specific method of the claimed "in vivo selection".

The art also does not teach methods of "in vivo selection" (i.e. selection of a specific antigen from a plurality of different antigens that can elicit an immune response inside an animal). The instant claimed methods are analogous to a method of identifying one single entity from a plurality of different entities (e.g. hundreds, thousands, or millions of entities) within one confinement. Without identifiable tags (or other feasible identifications) for each single entity within the plurality, one cannot "identify" or "select" a single specific entity out of the pool of plurality of entities that could have caused the phenomenon of interest. That is it is logically impossible to "fish out" one specific antigen out of a pool of different antigens based on a general immune response to the pool of antigens by the animal, because any one of the antigens could have possibly caused the immune response in the animal. This is evidenced by applicant's own publication (Barry et al., Nature. Vo. 377: 632-635; 10/1995). In the publication, the reference states "The protection offered by both libraries indicates that there must be several different protective plasmids in each. Preliminary tests of two 69-member sibs ... gave no protection, suggesting that the protective plasmid(s) ... are located else where in the library." (p. 635, left col, last para). The above said statement indicates that one would not be able to identify which member(s) (or plasmid(s)) of the library elicited the immune response in the animal without any further testing outside the animal.

Even if a specific member (a specific antigen) is identified to elicit an immune response in an animal, it would still require further experimentation to determine if the said member can provide protection against the pathogen from which the antigen is derived. The art does not teach that any nucleic acid or antigen can be used as a vaccine for protection against any pathogen. For example, Ciprian et al (Achives of Medical Research. Vol. 25(2): 235-239; 1994), teach that none of the tested vaccines (cell suspension containing nucleic acids) provided complete protection against a specific type of Mycoplasma (p. 238, bottom of right col.).

Furthermore, the instant claimed scope encompasses various pathogens including viruses, bacteria, fungi, etc. It is not known in the art that there is a successful vaccine for each type of pathogen. For example, a successful vaccine has not been developed for HIV, especially for vaccinating human. Further, there is no generalized method that would allow routine transfer the results of vaccine testing in animals for certain pathogens (such as mycoplasmas) to be utilized for human vaccines. For example, Crystal (Science. Vol. 270: 404-409; 10/20/1995; cited in IDS) teaches that many problems exist for introducing nucleic acid containing material (such as the nucleic acid vaccine of the instant application) into human, and there are no simple solution to these problems (p. 409 of the reference). Thus, vaccination using nucleic acid material in animals (especially in human) is highly unpredictable.

Additionally, the in vitro data provided given the unpredictability of the art would not be viewed as correlative to human applications. In vivo application necessarily involves unpredictability with respect to physiological activity of an asserted process in humans. See discussion in Ex parte Kranz, 19 USPQ2d 1216,1218-1219 (6/90).

Therefore, the state of the art for identifying specific antigens from a plurality of antigens within an inoculated animal, and vaccinating various subjects with various antigens against different pathogens are highly unpredictable. Although there are positive initial indications for the feasibility of using certain antigens in certain animals (including human), there is no general demonstration of successful screening and vaccination methods conducted variously.

The level of one of ordinary skill

The level of skill would be high, most likely at the Ph.D./MD level.

The amount of direction or guidance present and the presence or absence of working examples

In the present instance, the only working example provided are injecting a plurality of members (antigens or nucleic acids) into an animal, and determining if the plurality (not any one single antigen) that has elicited an immune response (e.g. Example 2 of the spec.). The only working example for vaccinating a subject is a vaccine composed of a plurality of antigens (not one particular antigen or nucleic acid; e.g. Example 2 of the spec.). Accordingly, the specification discloses only limited examples that are not representative of the claimed genus of peptides.

The quantity of experimentation needed

Due to the unpredictabilities of the so-called "in vivo selection" method and vaccination in various "subjects" (as discussed supra), and the lack of guidance in the instant specification, undue experimentation would be required. Given the complications or mixed results of "in vivo"

screening and vaccinations of various subjects using different antigens, undue experimentation would be required. Because the art does not provide successful and general methods of screening for every antigen from any pathogen, and vaccinating any subject with any antigen, undue experimentation such as trial-and-error process would have to be employed for identifying various specific antigens from a pathogen, and developing various vaccines for different subjects to protect against various pathogens.

Conclusion

Due to the non-routine of experimentation necessary to determine the feasibility in vivo screening and developing vaccines for various pathogens; the lack of direction/guidance presented in the specification regarding the specific requirements for such methods; the unpredictability of the in vivo screening, and vaccinating methods as established by the state of the prior art; the breadth of the claims, undue experimentation would be required of a skilled artisan to make and/or use the claimed invention in its full scope.

Second paragraph of 35 U.S.C. 112

26. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

27. Claims 41, 43-45, 47-60, 62, and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 recites "obtaining a nucleic acid", "wherein the nucleic acid ... has been determined to elicit an immune response", "identify said nucleic acid", "administering the nucleic acid", which claim language interpreted in light of the instant specification can be broadly and reasonably construed to mean a method of using the claimed "nucleic acid". However, applicants assert in the Reply, filed on 2/1/07, p. 5, that the Action is inaccurate in interpreting the "nucleic acid" has elicited the immune response, "rather than an antigen encoded by a nucleic acid". Thus, it is not clear which component the claimed method requires.

Claim 41 recites "in vivo selection", which can be interpreted variously, and is not clearly defined in the instant specification. One of ordinary skill in the art would not be able to apprise the metes and bounds of the claimed method steps.

Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: the nexus between the "nucleic acid" and the "member" from the library. It is not clear from the claim language if the obtained "nucleic acid" is the same as the selected "at least first member" from the library. Claim 41 recites "a library comprising DNA or RNA sequences", which does not dictate that the "obtained" "nucleic acid" is a member of the said library. Thus, one of ordinary skill in the art would not be able to define the metes and bounds of the claimed method.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Art Unit 1639
4/10/07

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PRIMARY EXAMINER